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Family Cancer Forum

Breast Cancer Risk Lowered After Removing Ovaries

A collaborative team of researchers, led by the group at the University of Pennsylvania Cancer Center, recently found that women with mutations in BRCA1 reduced their breast cancer risk by up to 70% after having their ovaries removed. Since women with mutations in the breast cancer susceptibility genes BRCA1 and BRCA2 have an increased chance of developing both breast and ovarian cancer, and since screening for early stage ovarian cancer has never been proven to be effective, many women decide to have their ovaries surgically removed by a procedure called *prophylactic oophorectectomy*. This surgical procedure removes healthy ovaries in the hopes of reducing the risk of ovarian cancer.

This study, recently published in the *Journal of the National Cancer Institute*, provides women with additional important information to use when making the difficult decisions about how to best deal with their cancer risks. Many experts in cancer genetics have already started to recommend prophylactic oophorectomy to women with BRCA mutations who have completed having their families. Ovarian cancer is difficult to treat effectively when it is not found in the early stages, and unfortunately, most of the time it isn't. For high risk women, the prophylactic oophorectomy has the added benefit of lowering breast cancer risk, in addition to providing protection from ovarian cancer.

This results of this study were made possible only by the generous contributions of time and information by women participating in this study through the University of Pennsylvania Cancer Center, Creighton University, Dana Farber Cancer Institute, Fox Chase Cancer Center and the University of Utah. Women with BRCA1 mutations who had prophylactic oophorectomies were considered "subjects." Women in the "control" group of women,

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Penn Joins National Cancer Genetics Network

The University of Pennsylvania Cancer Center was recently selected a founding member of a new, collaborative group, The National Cancer Genetics Network, a national effort to help researchers better understand what causes cancer and how to improve its detection, prevention, and treatment. Since researchers are most interested in studying families with a history of cancer, and often need more participants than any one cancer research center can enroll, the national network hopes to increase the number of study participants for certain research projects. The national network is made up of eight major sites, each selected by the National Cancer Institute for the excellence in cancer genetics. Each site will invite people to enroll who may be willing to be in future cancer research studies.

Combining people from all of the network sites will make it possible for the research to happen more quickly and effectively. The national Network will also contribute to cancer research by gathering some basic medical and family history information about each participant. This information will be updated every year and may be useful in answering some basic research questions about cancer and genetics.

You may be invited to join in the local network if:

- You have had breast, ovarian, colon, rectal, or prostate cancer; or
- You have one of several rare forms of cancer known to be hereditary; or

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Breast Cancer Risk Lowered After Removing Ovaries

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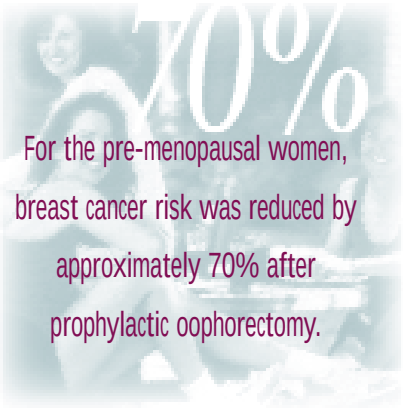

consisting of women with BRCA1 mutations who had not had this surgery. The risk of breast cancer was compared between the subject and control groups. The women in the subject group were followed for an average of ten years, and all cases of breast cancer were recorded. The overall reduction in breast cancer risk for those who had the surgery, was 53% compared to those who did not have the surgery. Prophylactic oophorectomy reduced breast cancer risk most dramatically in women who were pre-menopausal at the time of their surgery. For the pre-menopausal women, breast cancer risk was reduced by approximately 70% after prophylactic oophorectomy. While not specifically measured in this study, researchers expect to find that women who have already had one breast cancer, will have a lowered risk of developing a second breast cancer after prophylactic oophorectomy as well.

Women who are deciding about prophylactic oophorectomy often are concerned about how this surgery will affect their overall quality of life, and risk for other health problems. Ovaries provide a woman with her major source of estrogen. Following a prophylactic oophorectomy, women enter into menopause. Lack of estrogen may then lead to symptoms such as hot flashes, and an increased risk for heart disease as well as osteoporosis, a condition where bones become weakened and brittle. An important consideration for women who have not yet reached menopause naturally is what to do about hormone replacement therapy after having a prophylactic oophorectomy.

Researchers in this study examined women who used hormone replacement therapy (HRT) following their prophylactic oophorectomy, as well as those who did not. The researchers found that the use of HRT did not affect the significant reduction in breast cancer risk.

Researchers are continuing to study this group of women who have had prophylactic oophorectomies to monitor long term health effects. It is hoped and anticipated that in the future, there will be additional options for women with BRCA alterations to lower the risk of developing cancer.

Protection from Health Insurance Discrimination—HIPAA

Fears of losing one's health insurance, or having rates raised, have deterred some people from taking advantage of genetic testing that might otherwise provide helpful medical information. Men and women have been concerned that if an insurance company learned about the presence of a cancer predisposing gene, their insurability status would be significantly affected. Fortunately, after several years of experience with testing, and the implementation of state and federal legislation, there is little evidence that health insurance companies are using genetic testing to discriminate against women and their families.

In 1996, a new federal law was passed, called "The Health Insurance Portability and Accountability Act," or HIPAA. The law, which took effect in 1997, prevents group health insurers from limiting employees coverage, or denying a new employee coverage, due to a pre-existing condition, as long as a person has had continuous group health coverage up to that point. A pre-existing condition can be something like heart disease, diabetes, or cancer. This new law also includes information from genetic tests under the same protection as a pre-existing condition.

A woman with breast cancer, for example, who has been on her own or her partner's group health insurance policy, can not be dropped, or charged a different rate, or denied access to a new group health plan when she takes a new job. HIPAA makes it illegal for the new employer to not cover any breast cancer-related treatment for a certain time period — as had been the case in the past for some people with pre-existing conditions like breast cancer. However, a

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Coping with Cancer Risk— Most Women Doing Fine

It is the hope that genetic testing information will continue to become increasingly valuable when tailoring medical care. The information can be used to determine risk for cancer, or in some cases second cancers, in families with gene alterations or mutations.

Appropriate medical care recommendations can then be made that are individualized to a person's level of risk. However, there may be some negative aspects to receiving information about the risk of developing cancer. Researchers have been concerned that some people might become stressed after learning about their cancer risk, or the risk of an additional cancer. And for some, this worry might lead to depression, or other serious psychological outcomes.

Many of you have been participants in a study led by Jim Coyne, PhD, a psychologist at the University of Pennsylvania Cancer Center and formerly at the University of Michigan. Dr. Coyne's detailed surveys and telephone interviews have led to some fascinating and reassuring findings about how women from high risk breast cancer families are coping.

Many of you will recall answering detailed questions about stress, coping, and symptoms of depression over the telephone. The results from your valuable contributions to this study are now being published in the *Journal of Consulting and Clinical Psychology,* a leading scientific journal that will help inform health care providers working with hereditary breast and ovarian cancer families.

The research sample for this study consisted of 464 women. The majority of women were in their late forties, and were predominantly white, christian, married, with an average of two children. About half of the women in this study have been diagnosed with breast cancer in the past, and about half are at high risk, but have been cancer free. A very significant finding is that there was no difference in levels of distress among women who have, and have not been diagnosed with breast or ovarian cancer.

Women who were found to have significant levels of depression or other psychological problems were referred to the appropriate resources. However, the number of women in this group was small overall, and consistent with what a researcher would expect to find in the general population.

While these results are reassuring, they do not imply that women in these circumstances do not have stress specifically related to their cancer, and their cancer risk, but they do suggest that most women are finding ways of coping with their stress. Dr. Coyne compared rates of distress in women from the high-risk breast/ovarian cancer research group with those of women waiting for an appointment in their primary care doctor's office. He actually found lower rates of distress in the high-risk research group than in women from the waiting room group.

Dr. Coyne's study has been among the most comprehensive study of its type so far. It provides good evidence that the majority of women are coping well, despite the challenges that come from being a member of a hereditary cancer family. Dr. Coyne describes the research participants as a "remarkably resilient group of women." This research will be continuing as more women in the research group as well as in the general community receive genetic testing results.

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Tamoxifen Reduces Breast Cancer Risk by 49%

Recent results from The Breast Cancer Prevention Trial (BCPT), a large national study, indicate that women taking Tamoxifen for an average of four years had a 49% reduction in breast cancer incidence, compared with women who were taking a placebo (inactive sugar pill). John Glick, MD, the director of the University of Pennsylvania Cancer Center could hardly contain his excitement when he learned of the news. For those who regularly treat women with breast cancer, the idea of being able to provide women with a way to prevent this disease from occurring at all is more that just appealing, and seems nothing short of miraculous.

Tamoxifen, also known by its trade name Nolvadex®, is not a new medication. For over twenty years, it has been used to treat women with breast cancer. Because of the early positive result, the BCPT investigators working with the National Surgical Adjuvent Breast and Bowel Project with support from the National Cancer Insitute made the dramatic decision to end this trial early. This way, the 13,388 participating women would know whether they were taking tamoxifen or the placebo, and could consider starting tamoxifen therapy after consulting with their personal physician.

Taking tamoxifen did increase the chance of developing three rare but serious health problems. In the study group of over 13,000, there were 36 cases of endometrial (uterine) cancer among those taking tamoxifen, compared to 15 cases in the placebo group. There were 18 cases of pulmonary embolism (blood clot in the lung) in the tamoxifen group versus six cases in the placebo group, and 35 cases of deep vein thrombosis (blood clots in major veins) in the tamoxifen group versus 22 cases in the placebo group. Although these side effects are uncommon and in many cases treatable, it is nonetheless extremely important for every woman considering taking tamoxifen to carefully consider the risks and benefits with her physician.

The BCPT looked for other possible benefits to tamoxifen, in addition to the reduction in breast cancer risk. There was no difference in the number of heart attacks between the tamoxifen and the placebo group. However, women in the tamoxifen group did have fewer bone fractures of the hip, wrist and spine. Women who took tamoxifen were also shown to had 50% fewer diagnoses of non-invasive forms of breast cancer, such as ductal or lobular carcinoma in situ.

The NSABP is actively conducting the next breast cancer prevention study called the STAR trial, which will compare a newer medication called raloxifene to tamoxifen. Women in this study will be randomly assigned to one or the other medication; there is no placebo group in this new trial. For more information on the STAR trial, see page 5.

Protection from health Insurance Discrimination

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woman with breast cancer who has not been covered by any health insurance policy for the last year IS subject to wait up to six months *is* until her new insurance coverage will cover any expenses related to any pre-existing condition, including breast cancer.

So what does this mean for individuals with a BRCA1 or BRCA2 gene alteration? It means, if you are in a group health plan, you canÌt be dropped, or have your rates increased, even if your insurer learns about your genetic test result. If you have a BRCA1 or BRCA2 alteration, and continue to be covered in a group health plan, you canÌt be charged a different rate as someone else in the same group. If you work in an office of 200 people, for example, everyone in the group will pay the same rate. For group health insurance, the insurer canÌt charge someone in the group a higher or lower rate, based on good or poor health, or genetic test results. HIPAA also makes it illegal for someone with a BRCA1 or BRCA2 alteration to be singled out and denied access to the same plan offered to all other employees.

There are some limitations to HIPAA — it does not protect people who buy their own individual health insurance policies. For example, a woman who does free-lance consulting, who buys her own individual plan, is not protected under HIPAA. Fortunately, over 90% of Americans with health insurance are insured through group health plans, so this important protection is there for a very significant majority of people. We will continue to work with policy makers, legal experts, politicians and legislators to ensure that no one is left out of the loop of protection. After all, no one should have to choose between receiving access to valuable health information, and access to health insurance.

If you feel you have been discriminated against based on genetic testing, please let us know by calling Jill Stopfer, MS at 215-349-8143.

Preventing Breast Cancer—The STAR Trial

The results of the first major breast cancer prevention study in the country are in — and they are quite exciting. The medication called tamoxifen has been shown to reduce a healthy woman's chances of ever developing breast cancer by 49%. (see accompanying story about tamoxifen on page 4 .) As a follow-up to this major study, a new study, called STAR, (Study of tamoxifen and raloxifene) has recently begun to compare the effectiveness of tamoxifen versus another medicine called raloxifene.

The STAR trial, conducted by the NSABP (National Surgical Adjuvant Breast and Bowel Project), will enroll 22,000 post-menopausal women age 35 and older who are at increased risk of developing breast cancer. Women will randomly be assigned to take either raloxifene or tamoxifen for five years. This will be a double blind study, meaning that no one will know which medicine the participant is taking until the trial is completed. Study participants will receive close follow-up examinations, including a mammogram, physical exam, and gynecologic exam on a regular basis for at least five years.

Raloxifene, also known as Evista, is one of a new class of drugs called selective estrogen receptor modulators, or SERMs. These drugs have also been referred to as "designer estrogens," since they offer some of the same positive effects of estrogen by preserving bone density and offering protection from heart disease. However, unlike traditional estrogen replacement therapy, raloxifene has not been associated with small increases in risk for breast and uterine cancer. raloxifene has already received approval from the US Food and Drug Administration (FDA) for the prevention of osteoporosis, a condition where bones become weakened and brittle.

Early evidence that raloxifene can offer protection from breast cancer comes from a two year study of 7,705 postmenopausal women being treated for osteoporosis. Women at average risk of developing breast cancer reduced their chance of developing the disease by 66% with daily use of raloxifene, compared to the control group. In another analysis, looking at information on just over 10,000 women from nine different trials investigating the drug's safety, raloxifene was associated with a 55% reduction in the risk of developing breast cancer.

Eligibility for the STAR trial will be determined by participating centers using the National Cancer Institute's Risk Assessment Tool, also known as the Gail Model. Women who are determined to have at least a 1.7% chance of developing breast cancer within the next five years will be eligible. The NSABP has already selected 193 institutions to participate in this study, including the University of Pennsylvania Cancer Center. Additional institutions have been selected to affiliate with the study institutions, so a total of 400 active enrollment centers in 48 states, and 6 Canadian provinces will participate in the STAR trial. This study is also supported by the National Cancer Institute.

Women from any part of the country who are interested in learning more about the STAR trial, and possibly enrolling can contact the University of Pennsylvania Cancer Center at 1-800-789-PENN for a referral to a local participating center. The STAR trial nursing coordinator at the University of Pennsylvania Cancer Center, Patty O'Neill, can be reached at 1-800-789-PENN. Additional information about the STAR trial can be found through the NSABP website at http://www.nsabp.pitt.edu.

Breast Cancer Prevention for Young Women

A new study was recently opened at the University of Pennsylvania Cancer Center, specifically for young women at increased risk of developing breast cancer. This study has been will be testing medications that may help make mammograms easier to read by reducing breast density. This effect may in turn also reduce the risk of developing breast cancer. Participants in this research study would use a daily nasal spray containing the hormones Deslorelin®, estradiol and testosterone.

One goal of this study is earlier recognition of any abnormality of the breast tissue. Young, pre-menopausal women typically have denser breast tissue than older women. This can limit the effectiveness of mammography, since areas of high density could mask an underlying breast problem. While mammograms are not perfect, they are still useful in evaluating the breast tissue of young women. This study may be able to improve the sensitvity of mammograms in young high risk women. Response to the medications will be assessed by measuring blood hormone levels, and mammographic breast density.

As with other prevention studies, investigators will carefully monitor all participants for possible side effects from the study. Radiology studies will be used to assess the bones for any changes in bone

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African American Women and Breast Cancer

African American women develop breast cancer at similar rates to American Caucasian women. However, more African American women are diagnosed with breast cancer under the age of 50 than Caucasian women. In addition, African American women have lower rates of survival from breast cancer than other women. So far, little is known about the role of family history, and breast cancer risk genes in women of African descent. The majority of work done so far to try to understand the genetic, or inherited factors that underlie breast cancer risk have been done in Western European, Caucasian women.

Fortunately, researchers are now focusing attention on a broader sample of women in many different studies. Researchers at the University of Pennsylvania Cancer Center are particularly interested in studying genetic cancer risk profiles in African American women. These profiles will be compared to information already collected on Caucasian women, and used to improve our ability to provide accurate risk assessment to African American individuals.

African American women, diagnosed with breast cancer at any age, will be studied to determine how often alterations in the breast cancer susceptibility genes BRCA1 and BRCA2 occur. It is known that different geographic and ethnic populations have different frequencies of having these alterations, but so far researchers do not fully understand how often African American families develop breast and/or ovarian cancer due to these genes. Researchers will also be studying genes that confer a lower risk of breast cancer than BRCA1 or BRCA2. These other risk genes, which modify breast cancer risk to a smaller degree, are involved in hormone metabolism and DNA repair.

By gaining a better understanding of the underlying genetic factors that influence breast cancer risk in African American women, researchers hope to gain insights into several important questions. African American women tend to have poorer prognoses when diagnosed with the same forms of breast cancer as Caucasian women. If genetic factors can be identified to explain this difference, then researchers hope that treatments can be specifically developed to address the source of breast cancer risk in these women.

African American women with breast cancer who are interested in contributing to this study should contact Kathy Calzone, RN, MSN at 215-349-8141 for further information. There is no cost to participate in this study and travel to the University of Pennsylvania is not necessary.

Family Research UPDATE

The Cancer Genetics Research Program is continuing to gather information aimed at understanding how people cope with information about their cancer risks; how people understand information offered about these risks; and their response to strategies to deal with increased risk.

Many participants who live at a significant distance from University of Pennsylvania have received genetic testing information from a local provider, such as an oncologist, family doctor or nurse, genetic counselor or other health professional. We are interested in knowing how these sessions went, and how satisfied participants were with the information provided. Surveys were sent to all of you who received genetic test results from your local provider. Please consider filling yours out and sending it back, if you haven't done so already. Your participation in this and other studies will help determine how these important services are delivered in the future at the University of Pennsylvania and other cancer genetics centers across the country. Thanks again for your continued participation, for those of you who have sent your surveys back.

The research laboratory of Barbara Weber, MD is continuing to test a large number of research blood samples from participants from all over the world. Some of you who have been waiting for results to come back should be hearing from the University of Pennsylvania in the near future. Those individuals participating in research projects who are eligible to receive their results locally will receive a letter from us as soon as the information is available. All research participants with completed genetic testing results receive the same letter - it's not possible to tell whether a mutation has been found or not based on this first letter, indicating results are available.

We've found that some people have chosen not to receive their genetic test results, while others have delayed receiving their results for a year or more. Of course, many of you want to learn your results as quickly as possible. We will make every effort to provide you with this information in as timely a manner as possible. We understand that the waiting can be difficult. All research participants are always welcome to contact us here at 215-898-0247 to check on the status of your genetic testing results. Again, thank you for your patience, and for participating in studies that will greatly assist us in understanding hereditary breast and ovarian cancer.

High Risk Prostate Cancer Families

It has been observed for many years that prostate cancer, like breast and ovarian cancer, can run in families. Unfortunately, even less is understood about hereditary prostate cancer than about hereditary breast and ovarian cancer. While some of the important genes (BRCA1 and BRCA2) underlying hereditary breast and ovarian cancer have been isolated, this is not yet the case for prostate cancer. In particular this is because it is more difficult to distinguish between hereditary and non-hereditary cases of prostate cancer than it is for hereditary and non-hereditary cases of breast cancer. For example, while the ages of diagnosis may be dramatically earlier in women with hereditary breast cancer as opposed to non-hereditary breast cancer, this may not be the case for hereditary versus non-hereditary prostate cancer.

We would like to learn more about familial prostate cancer, so that we can better define some of the genetic changes that underlie the development of prostate cancer. We are therefore interested in locating prostate cancer families with 3 more men with prostate cancer - 2 of whom have been diagnosed under age 55 or with men affected with prostate cancer in 3 generations to participate in a research study. If you would be interested in participating in this research study or would like more information about hereditary prostate cancer please call Jennifer Farmer, MS in the Division of Medical Genetics at 215-662-4740.

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1999 FAMILY HISTORY UPDATE FORM

We request that all participants in the Cancer Risk Evaluation Program and all research participants, whether or not you have ever given a blood sample, or whether or not you have any specific changes to report, complete and send in your updated information. This way, you may be contacted when a study relevant to your family becomes available. These updates provide critical research information - thank you for your help!

Your Name: _____ Date of Birth: _____

Address: _____
(street address, apt. no., etc.) (city) (state) (zip code)

Phone: (Home) _____ (Work) _____

Ethnicity on mother and father's side _____
(eg. Italian, Irish, Jewish): (Mother's side) (Father's side)

Has anyone in your family developed cancer in the last 12 months? [ ] No [ ] Yes (If yes, please complete the following:)

Name	Names of parents	Type of cancer	Date or age at diagnosis

Has anyone in your family had prophylactic (preventive) surgery? (removing healthy breasts or ovaries to prevent cancer) [ ] No [ ] Yes
(If yes, please complete the following:)

Name _____ Type of surgery _____

Date or age at surgery _____ Names of parents _____

Name _____ Type of surgery _____

Date or age at surgery _____ Names of parents _____

Have there been any births or deaths in your family in the last 12 months? [ ] No [ ] Yes (If yes, please complete the following:)

Name _____ Date of birth or date of death _____

Names of parents _____ (If Applicable) Cause of death _____

Name _____ Date of birth or date of death _____

Names of parents _____ (If Applicable) Cause of death _____

Has anyone else in the family had genetic testing outside of University of Pennsylvania? (note: this information stays in CONFIDENTIAL research charts) Yes [ ] No [ ] Unsure [ ] Prefer not to disclose this information [ ]

If so, who? _____ Relationship to you _____
(name) (e.g. maternal cousin, paternal uncle)

If so, who? _____ Relationship to you _____
(name) (e.g. maternal cousin, paternal uncle)

Genetics Network

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- You are closely related to someone who has had one of these cancers.

At the University of Pennsylvania Cancer Center, we hope to enroll at least 1,000 individuals into the local network. Once a participant has been enrolled in the local network, we will determine whether to send your information, *without* any personal identifying information, to the national network based upon such factors as a family history of cancer.

The national collaborative effort is expected to provide additional research participation opportunities to families all over the country. It is hoped that the cooperation in the Cancer Genetics Network will advance research in this important arena more quickly than any of the major cancer genetics centers could working on their own. We will be in contact with many of our participants with more information about joining the Cancer Genetics Network.

Breast Cancer Prevention for Young Women

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density, a sampling of the lining of the uterus will be taken to monitor for abnormal changes. In addition, participants will be asked to complete a symptom survey and a quality of life questionnaire. This study is being conducted at four sites around the country, including City of Hope National Medical Center in Duarte, CA; Dana Farber Cancer Institute in Boston, MA; and the University of Chicago, IL, as well as University of Pennsylvania Cancer Center.

You may be eligible for this study if you are pre-menopausal, between the ages of 21 and 39, have never been diagnosed with any form of cancer, and have an increased risk of breast cancer. A woman may be determined to be at increased risk of developing breast cancer because she has a BRCA1/2 alteration, or is at increased risk of breast cancer based on your family history. A formal risk assessment must be completed to determine eligibility, and lifetime risk of breast cancer must be at least 30%. The average woman by contrast, has an approximately 11% lifetime chance of developing breast cancer. If you would be interested in learning more about this study, please contact Kathy Calzone, RN, MSN at 215-349-8141.

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